CLAIMS

What is claimed is:

1. A pharmaceutical composition comprising:

a DNA methylation inhibitor; and

an anti-neoplastic agent whose activity as an anti-neoplastic agent in vivo is adversely affected by aberrant DNA methylation.

2. The pharmaceutical composition according to claim 1, wherein the DNA methylation inhibitor is a cytidine analog.

3. The pharmaceutical composition according to claim 2, wherein the cytidine analog is decitabine.

4. The pharmaceutical composition according to claim 1, wherein the anti-neoplastic agent is selected from the group consisting of alkylating agent, antibiotic agent, retinoid, antimetabolic agent, hormonal agent, plant-derived agent, anti-angiogenesis agent and biologic agent.

5. The pharmaceutical composition according to claim 1, wherein the anti-neoplastic agent is an alkylating agent selected from the group consisting of bischloroethylamines, aziridines, alkyl alkone sulfonates, nitrosoureas, nonclassic alkylating agents and platinum compounds.

6. The pharmaceutical composition according to claim 1, wherein the DNA methylation inhibitor is decitabine and the anti-neoplastic agent is cisplatin or carboplatin.

7. The pharmaceutical composition according to claim 1, wherein the anti-neoplastic agent is an antibiotic agent selected from the group consisting of doxorubicin,

daunorubicin, epirubicin, idarubicin and anthracenedione, mitomycin C, bleomycin, dactinomycin, and plicatomycin.

8. The pharmaceutical composition according to claim 1, wherein the anti-neoplastic agent is an antimetabolic agent selected from the group consisting of fluorouracil, floxuridine, methotrexate, leucovorin, hydroxyurea, thioguanine, mercaptopurine, cytarabine, pentostatin, fludarabine phosphate, cladribine, asparaginase, and gemcitabine.

9. The pharmaceutical composition according to claim 1, wherein the anti-neoplastic agent is a hormonal agent selected from the group consisting of diethylstibestrol, tamoxifen, toremifene, fluoxymesterol, raloxifene, bicalutamide, nilutamide, flutamide, aminoglutethimide, tetrazole, ketoconazole, goserelin acetate, leuprolide, megestrol acetate and mifepristone.

10. The pharmaceutical composition according to claim 1, wherein the DNA methylation inhibitor is decitabine and the anti-neoplastic agent is tamoxifen.

11. The pharmaceutical composition according to claim 1, wherein the anti-neoplastic agent is a plant-derived agent selected from the group consisting of vincristine, vinblastine, vindesine, vinzolidine, vinorelbine, etoposide teniposide, paclitaxel and docetaxel.

12. The pharmaceutical composition according to claim 1, wherein the DNA methylation inhibitor is decitabine and the anti-neoplastic agent is a retinoid selected from the group consisting of all-trans-retinol, all-trans-retinoic acid, 13-cis-retinoic acid, and 9-cis-retinoic acid.

13. The pharmaceutical composition according to claim 1, wherein the anti-neoplastic agent is a biologic agent selected from the group consisting of immuno-modulating proteins, monoclonal antibodies, tumor suppressor genes, and cancer vaccines.

14. The pharmaceutical composition according to claim 13, wherein the immuno-modulating protein is selected from the group consisting of interleukin 2, interleukin 4, interleukin 12, interferon α interferon ß, interferon γ, erythropoietin, granulocyte-CSF, granulocyte, macrophage-CSF, bacillus Calmette-Guerin, levamisole, and octreotide.

15. The pharmaceutical composition according to claim 13, wherein the monoclonal antibody is selected from the group consisting of HERCEPTIN, RITUXAN, MYELOTARG, and CAMPATH.

16. The pharmaceutical composition according to claim 13, wherein the tumor suppressor gene is selected from the group consisting of *DPC-4, NF-1, NF-2, RB, p53, WT1, BRCA,* and *BRCA2.*

17. The pharmaceutical composition according to claim 13, wherein the cancer vaccine is selected from the group consisting of gangliosides, prostate specific antigen, α-fetoprotein, carcinoembryonic antigen, melanoma associated antigen MART-1, gp100, papillomavirus E6 fragment, papillomavirus E7 fragment, whole cells or portions/lysate of antologous tumor cells, and allogeneic tumor cell.

18. The pharmaceutical composition according to claim 1, wherein said composition is useful in the treatment of diseases associated with abnormal cell proliferation or abnormal angiogenesis.

19. The pharmaceutical composition according to claim 1, wherein the anti-neoplastic agent is ^{131}I.

20. A method for treating a disease associated with abnormal cell proliferation, comprising:

administering to a patient having the disease a therapeutically effective amount of a DNA methylation inhibitor, in combination with an therapeutically effective amount of

an anti-neoplastic agent whose activity as an anti-neoplastic agent in vivo is adversely affected by aberrant DNA methylation.

21. The method according to claim 20, wherein the disease associated with abnormal cell proliferation is selected from restenosis, benign tumor, cancer, hematological disorder and atherosclerosis.

22. The method according to claim 21, wherein the benign tumor is selected from the group consisting of hemangiomas, hepatocellular adenoma, cavernous haemangioma, focal nodular hyperplasia, acoustic neuromas, neurofibroma, bile duct adenoma, bile duct cystanoma, fibroma, lipomas, leiomyomas, mesotheliomas, teratomas, myxomas, nodular regenerative hyperplasia, trachomas and pyogenic granulomas.

23. The method according to claim 21, wherein the cancer is selected from the group consisting of breast cancer, skin cancer, bone cancer, prostate cancer, liver cancer, lung cancer, brain cancer, cancer of the larynx, gallbladder, pancreas, rectum, parathyroid, thyroid, adrenal, neural tissue, head and neck, colon, stomach, bronchi, kidneys, basal cell carcinoma, squamous cell carcinoma of both ulcerating and papillary type, metastatic skin carcinoma, osteo sarcoma, Ewing's sarcoma, veticulum cell sarcoma, myeloma, giant cell tumor, small-cell lung tumor, gallstones, islet cell tumor, primary brain tumor, acute and chronic lymphocytic and granulocytic tumors, hairy-cell tumor, adenoma, hyperplasia, medullary carcinoma, pheochromocytoma, mucosal neuronms, intestinal ganglloneuromas, hyperplastic corneal nerve tumor, marfanoid habitus tumor, Wilm's tumor, seminoma, ovarian tumor, leiomyomater tumor, cervical dysplasia and in situ carcinoma, neuroblastoma, retinoblastoma, soft tissue sarcoma, malignant carcinoid, topical skin lesion, mycosis fungoide, rhabdomyosarcoma, Kaposi's sarcoma, osteogenic and other sarcoma, malignant hypercalcemia, renal cell tumor, polycythermia vera, adenocarcinoma, glioblastoma multiforma, malignant melanomas, and epidermoid carcinomas.

24. The method according to claim 21, wherein the hematological disorder is selected

from acute myeloid leukemia, acute promyelocytic leukemia, acute lymphoblastic leukemia, chronic myelogenous leukemia, chronic lymphoblastic leukemia, Hodgkins disease, Non-Hodgkin Lymphomas, the myelodysplastic syndromes, and sickle cell anemia.

25. The method of claim 20, wherein the disease is non-small cell lung cancer and the DNA methylation inhibitor is decitabine.

26. The method of claim 20, wherein the DNA methylation inhibitor is decitabine and the anti-neoplastic agent is a retinoid.

27. The method of claim 20, wherein the DNA methylation inhibitor is decitabine and the anti-neoplastic agent is a hormonal agent.

28. The method of claim 20, wherein the DNA methylation inhibitor is decitabine and the anti-neoplastic agent is cisplatin or carboplatin.

29. The method of claim 20, wherein the DNA methylation inhibitor is administered subcutaneously or intravenously.

30. The method of claim 20, wherein the DNA methylation inhibitor is decitabine and is administered intravenously or subcutaneously.

31. The method of claim 30, wherein decitabine is administered to the patient intravenously per day at a dose ranging from 1 to 100 mg/m^2.

32. The method of claim 30, wherein decitabine is administered to the patient intravenously per day at a dose ranging from 2 to 50 mg/m^2.

33. The method of claim 30, wherein decitabine is administered to the patient intravenously per day at a dose ranging from 5 to 20 mg/m^2.

34. The method of claim 30, wherein decitabine is administered to the patient intravenously per day for at least 3 days per treatment cycle at a dose ranging from 1 to 100 mg/m^2.

35. The method of claim 20, wherein the DNA methylation inhibitor is administered prior to the administration of the anti-neoplastic agent.

36. A kit for treating a disease associated with abnormal cell proliferation, comprising:

a container that contains decitabine and an anti-neoplastic agent whose activity as an anti-neoplastic agent in vivo is adversely affected by aberrant DNA methylation.

37. The kit according to claim 36, wherein the anti-neoplastic agent is a retinoid.

38. The kit according to claim 36, wherein the anti-neoplastic agent is cisplatin or carboplatin.

39. The kit according to claim 36, wherein the anti-neoplastic agent is a hormonal agent.

40. The kit according to claim 39, wherein the hormonal agent is selected from the group consisting of diethylstibestrol, tamoxifen, toremifene, fluoxymesterol, raloxifene, bicalutamide, nilutamide, flutamide, aminoglutethimide, tetrazole, ketoconazole, goserelin acetate, leuprolide, megestrol acetate and mifepristone.

41. The kit according to claim 39, wherein the anti-neoplastic agent is a monoclonal antibody selected from the group consisting of HERCEPTIN, RITUXAN, MYELOTARG, and CAMPATH.